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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/585,448

11/28/2006

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EXAMINER

YOUNG, SHAWQUA

ART UNIT

PAPER NUMBER

1626

NOTIFICATION DATE

DELIVERY MODE

03/02/2010

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

chalin@smithpatent.com

<b>Office Action Summary</b>	<b>Application No.</b> 10/585,448	<b>Applicant(s)</b> VAN DER SCHAAF ET AL.	
	<b>Examiner</b> SHAWQUIA YOUNG	<b>Art Unit</b> 1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 17 November 2009.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-34,37-40,43 and 44 is/are pending in the application.
- 4a) Of the above claim(s) 1-4,9-34,43 and 44 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 5-8 is/are allowed.
- 6) ☒ Claim(s) 37-40 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

Claims 1-34, 37-40, 43 and 44 are currently pending in the instant application. Claims 5-8 are allowed, claims 37-40 are rejected and claims 1-4, 9-34, 43 and 44 are withdrawn from consideration in this Office Action.

#### **I. *Response to Arguments***

Applicants' amendment, filed on November 17, 2009, has overcome the rejection of claims 37-40 under 35 USC 112, second paragraph as being indefinite for the term "Form B" and the rejection of claims 37-40 under 35 USC 112, second paragraph as being indefinite for being dependent on a non-elected claim. The above rejections have been withdrawn.

Applicant's arguments, filed November 17, 2009 with respect to the rejection of claims 37-40 under 35 USC 112, first paragraph as failing to comply with the enablement requirement and the rejection of claims 37-40 under 35 USC 102(b) as being anticipated by Sandquiet, et al. (GB 2315673A) have been fully considered but are not persuasive. Applicants argue that there is no evidence that the polymorphic form B of rizatriptan set forth in pending claims 37-40 is particularly sensitive or susceptible to polymorphic change in the course of pharmaceutical preparation. Applicants further argue that it is improper for the Examiner to simply presume, without further supporting evidence or specific indication in the art, that the presently claimed crystalline polymorphic form when it is processed to a medicament. However the Examiner wants to point out that according to the reference Haleblan, et al. (which is

Art Unit: 1626

cited in enablement rejection), that when creams are prepared and a metastable phase with high solubility is suspended in the cream base there is a high risk that nucleation of a more stable (less soluble) form will eventually occur (see page 912). The Halebian also teaches that using the wrong polymorph of a drug in aqueous vehicles can result in a phase conversion from the metastable to stable polymorph which produces crystal growth resulting in undesirable particle size distribution and caking, producing suspensions that cannot be uniformly resuspended by shaking (See page 912). Thus, the prior art reference provides support that it is well known that polymorphs when prepared in a pharmaceutical formulation can transition into another polymorph form because the original polymorphic form is not stable in formulation. It is also well known in the art that the use of water in preparing solutions with a polymorphic form of a compound can result in the transition to the free form of that compound. Applicants have failed to provide any support in the specification showing that the polymorph form B is a stable form and is present in that form after preparing a pharmaceutical formulation. The Examiner has provided clear support in the prior art that shows that polymorphs can change into another form during the formulation of a pharmaceutical composition. Therefore, it is Applicants' burden to show that the form B of rizatriptan is a stable form and does not change into another form during the formulation of a pharmaceutical composition. The Examiner has maintained the enablement rejection of claims 37-40. The Examiner has also maintained the 102b rejection of claims 37-40 because it is well known that water can be used as pharmaceutically acceptable carrier

Art Unit: 1626

and therefore when used in preparing a formulation with a polymorphic form can result in the free form of the compound which has already been taught in the prior art.

## II. ***Rejection(s)***

### ***Claim Rejections - 35 USC § 112, 1<sup>st</sup>***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 37-40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As stated in the MPEP 2164.01 (a), "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have need described. They are:

1. the nature of the invention,
2. the state of the prior art,

Art Unit: 1626

3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case, the claims are drawn to a pharmaceutical composition comprising an effective amount of a crystalline polymorphic form B.

### ***The nature of the invention***

A pharmaceutical composition comprising an effective amount of crystalline polymorphic form B.

### ***The state of the prior art***

The state of the prior art is that the preparation of pharmaceutical compositions requires creating solutions, milling, adding diluents, excipients, surfactants, etc. The process of preparing a pharmaceutical composition will cause a specific crystalline form, if in the metastable state to resort back to the most thermodynamically stable form which is the form with the lowest vapor pressure. Polymorphs tend to convert from less stable to more stable forms (Rouhi, page 32). It is also the state of the prior art that an acceptable carrier for a pharmaceutical formulation can be water. Dissolving a specific crystalline form in water, creating an aqueous solution, would put the compound in its free form and not in a crystalline form with a specific X-ray diffraction pattern. The use of a wrong polymorph of a drug when using an aqueous vehicle may provide a phase conversion from the metastable to stable polymorph (Haleblian et al., page 912).

***The predictability or lack thereof in the art***

The predictability or lack thereof in the art is that a metastable compound will resort back into its most thermodynamically stable form which would have a different X-ray diffraction pattern and also that a solution prepared from a specific crystalline form and water would contain the free form of the compound.

***The amount of direction or guidance present and the presence or absence of working examples***

While the specification has provided processes for the preparation of the crystalline forms D, the specification fails to provide the processes for preparing a pharmaceutical composition and to provide the steps of ensuring that the pharmaceutical compositions will maintain the specific forms as found in the specification and will not resort back to the free form or the most thermodynamically stable form of the compound.

***The breadth of the claims***

A pharmaceutical composition comprising an effective amount of crystalline polymorphic form B.

***The quantity of experimentation needed***

The quantity of experimentation needed is undue. One of ordinary skill in the art, without direction, would be unable to maintain a specific metastable crystalline form upon preparation into a pharmaceutical composition which may require milling or the formation of a solution.

***The level of the skill in the art***

While the level of skill in the art is high, one of skill in the art would be unable to maintain a specific metastable crystalline form upon the preparation of a pharmaceutical composition without direction and guidance which is not found in the instant specification. One of skill in the art would expect the pharmaceutical composition to contain the free form of the compound or the most thermodynamically stable form of the compound.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 37-40 are rejected under 35 U.S.C. 102(b) as being anticipated by *Sandquiet, et al.* (GB 2315673A). The instant invention claims a pharmaceutical composition comprising an effective amount of crystalline polymorphic form B.

The *Sandquiet, et al.* reference teaches rizatriptan benzoate and pharmaceutical compositions comprising thereof (example 8, page 18 and pages 19-21) and their use in treating migraines. This composition anticipates the composition comprising crystalline polymorphic form B of the instant invention because applicants are claiming a composition which could comprise for example water and dissolving a specific



crystalline form in water, creating an aqueous solution, would put the compound in its free form and not in a crystalline form with a specific X-ray diffraction pattern. Therefore, the composition would be identical as taught in the prior art.

### **III. Conclusion**

**THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shawquia Young whose telephone number is 571-272-9043. The examiner can normally be reached on 7:00 AM-3:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1626

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Shawquia Young/

Examiner, Art Unit 1626

/Rebecca L Anderson/

Primary Examiner, Art Unit 1626